ORIGINAL ARTICLE

BLOOD PRIME OF THE CARDIOPULMONARY BYPASS CIRCUIT IN CONGENITAL HEART SURGERY

Valdir Assis dos Reis Filho[1,2]*, José Cícero Stocco Guilhen[1], Mariana Leticia Matias[1], Karina Aparecida Antonelli Novello[1], Diego Gamarra Moreira[1], Jesus Antonio Gutierrez Saurith[1], Omar Alonzo Pozo Ibanez[1], Luiz Antonio Rivetti[2]

[1] Instituto Dante Pazzanese de Cardiologia, São Paulo, Brazil
[2] Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil

* **Corresponding author:** valdir_assisf@hotmail.com

Abstract

Introduction: *The use of cardiopulmonary bypass (CPB) is necessary during the repair of most congenital heart disease (CHD). The surface area of the CPB circuit and the volume of the filling prime are relatively large concerning the volume of neonatal and pediatric patients. Consequently, blood is often required to maintain an adequate haematocrit (HCT) level throughout the procedure.*

Objective: *To evaluate the effects of ultrafiltration (UF) of the blood prime from the cardiopulmonary bypass circuit in children undergoing surgical procedures to correct heart disease.*

Methods: *This is a prospective interventional study with convenience sampling of fifty-five children undergoing elective cardiac surgery that used CPB. Patients aged 0 to 10 years and ≤ 25kg were included in this study. The children were assigned to one of two groups as follows: control group (group 1) not using ultrafiltration of blood prime and experimental group (group 2) with UF of the prime before CPB. Blood samples were obtained for analysis of CPB circuit prime, during the intraoperative and after surgery in immediate postoperative period (IPO). The duration of mechanical ventilation (MV), intensive care unit (ICU) stay, and length of postoperative hospital stay were compared between the 2 groups.*

Results: *Levels of glucose, potassium and lactate values demonstrated a significant decrease after prime ultrafiltration in group 2, however an increase in sodium values was revealed (p= <0,001). In the present study, to postoperative clinical outcomes, there was not difference between groups in the duration of mechanical ventilation and ICU stay. However, length of postoperative hospital stay, group 1 demonstrated longer time in comparison with the group 2 [13 (6 – 35) vs 9 (6 – 34); Median (interquartile range) and p= 0.032]. Group 2 demonstrated lower lactate values in intraoperative and in the immediate postoperative period (p= 0.008). It was observed in the first postoperative 24 hours, stability in lactate levels between the groups.*

Conclusion: *Analysis of intraoperative and postoperative laboratory outcomes showed overall stability in blood parameters, with some specific variations in potassium and lactate levels. The observation of a shorter hospital stay in the group that had the prime ultrafiltration, it is suggested that this technique may help shorten the hospitalization period.*

Keywords: *Congenital heart defects, Ultrafiltration, Transfusion, Cardiopulmonary Bypass*

INTRODUCTION

Congenital heart disease (CHD) is characterized by malformation of the cardiac anatomy or the great intrathoracic vessels, causing significant cardiocirculatory alterations.[1,2] Congenital heart defects are one of the main causes of infant mortality in children under 1 year of age and are the result of an embryonic alteration of the heart's structure and function.[3] These defects are classified according to anatomical findings and present a wide variety of isolated and associated defects.[4,5] The majority of patients with CHD, around 80%, will require some cardiac procedure throughout their lives.[6] The surgery aims to increase survival and improve the quality of life of these individuals.[7,8]

The use of cardiopulmonary bypass (CPB) is necessary during the repair of most CHD. The surface area of the CPB circuit and the volume of the filling prime are relatively large concerning the volume of neonatal and pediatric patients. Consequently, blood is often required to maintain an adequate haematocrit (HCT) level throughout the procedure.[9,10,11]

High potassium levels, the presence of free hemoglobin, fragments of pro-inflammatory cytokines (IL-8 and TNF-α), and significant lactate concentration rates can be found in stored red blood cell (RBC) concentrates[9,10]. It is

essential to reduce the negative effects related to the addition of blood to the circuit and thus improve the postoperative outcome of patients. Washing the RBC used in CPB reduces the levels of metabolites and electrolytes. However, as far as attenuating the systemic inflammatory response syndrome (SIRS) is concerned, there is no conclusive data on whether the technique causes any major effects. [12, 13] The RBC has been associated with increased bleeding, longer hospital stays, and higher in-hospital mortality rates.[14]

Over the years, various approaches have been developed to mitigate the effects of blood prime during cardiopulmonary bypass, such as blood washing with recovery devices and pre-CPB ultrafiltration (UF). Among these, pre-bypass UF of the prime solution has proven to be a more feasible and straightforward strategy, as it does not require the use of additional materials or circuit modifications and is less likely to induce hemolysis. [15,16]

This study evaluated the potential benefits of ultrafiltration of the blood prime in the cardiopulmonary bypass circuit during surgical procedures in patients with congenital heart disease.

METHODS

This is a prospective, non-randomized interventional study with convenience sampling carried out in the Surgery Division of the Instituto Dante Pazzanese de Cardiologia (IDPC), located in the city of São Paulo — SP. This study was approved by the Research Ethics Committee under registration number CAAE: 53483721.0.0000.5462. Patients undergoing elective cardiovascular surgery using cardiopulmonary bypass were eligible for the study.

The patient selection process was based on convenience, depending on the availability of the surgical team, which determined the allocation into groups. Although the study was not randomized; the baseline characteristics of both groups were similar, minimizing the risk of selection bias. The study covered a population sample of individuals aged between 0 and 10 years and weighing < 25 kg. All underwent surgery to repair atrial septal defects (ASD), ventricular septal defects (VSD) and atrioventricular septal defects (AVSD). Patients in critical condition before surgery, with serious associated comorbidities, a known diagnosis of hematological diseases, and polytransfused patients were excluded from the study.

A careful selection of 55 children undergoing elective cardiovascular surgery was carried out, and the children's legal representatives were fully informed about the objectives and procedures of the research. In addition, all those responsible voluntarily agreed, formalizing their approval by signing the Informed Consent Form (ICF). The participants were divided into group 1 and group 2.

Anesthetic technique

General anesthesia in patients without peripheral access was induced under a face mask with 3% sevoflurane until venoclysis. Standard anesthesia was then performed with an intravenous infusion of midazolam 0.1-0.2 mg/kg, fentanyl 1-2 mcg/kg, and cisatracurium 0.15 mg/kg. After orotracheal intubation (OTI), radial artery punctures and central venous access were performed. Anesthesia was maintained with sevoflurane 1% and dexmedetomidine on a continuous infusion pump 0.2 to 0.7 mcg/kg/h. The total opioid dose during surgery was 10-20 mcg/kg, and midazolam 0.2 mg/kg was administered at the entrance and exit of the CPB, according to hemodynamic parameters.

CPB procedure

The CPB circuit was prepared in a standardized way for all patients. The equipment used consisted of: KIDS D100 or D101 hollow fiber oxygenator (Livanova, Mirandola, Italy), tube sets (Livanova, Mirandola, Italy), Revolution centrifugal pump (Livanova, Mirandola, Italy) and DHF 0.2 hemoconcentrator (Livanova, Mirandola, Italy). Cardiopulmonary bypass was started when the activated clotting time (ACT) exceeded 480 seconds.

Cardioplegia was administered using the Del Nido solution, prepared and delivered in a 1:4 blood-to-crystalloid ratio, at a temperature of 4°C. A single antegrade dose of 20 mL/kg was administered after aortic cross-clamping, with redosing considered only if the cross-clamp time exceeded 60 minutes. The Del Nido protocol was chosen due to its proven efficacy in myocardial protection during pediatric surgeries, allowing prolonged cardiac arrest with a single dose and reducing interruptions during the procedure. The patients were kept in moderate hypothermia (28°C) and the flow rates used varied between (100 mL/kg/min - 200 mL/kg/min), the pH-stat strategy was adopted throughout the procedure.

At the end of the procedure, the children were gradually rewarmed to 36.5º, and then aortic declamping was performed. After leaving cardiopulmonary bypass, protamine was administered to reverse the anticoagulant effect of heparin.

Ultrafiltration of prime

In all the children the prime consisted of Ringer's solution (300-500 mL), 100 IU/kg of heparin, and 10 mL of 8.4% sodium bicarbonate. The volume (in mL) of RBC that was used in the prime to provide the patient with a HCT of around 25% - 30% was obtained using the following equation:

$$\text{VOLUME} = \frac{[(\text{Volemia} * + \text{Prime}) \times \text{DesiredHCT}] - (\text{Volemia} * \times \text{CurrentHCT})}{0{,}6}$$

*Patient weight x 80
60= HCT of packed RBC

In both groups, blood was circulated at a temperature of 36.5°C for 5 minutes at a rate of 300 mL/min and then samples were taken to serve as a baseline. In group 1, blood was kept circulating until the onset of cardiopulmonary bypass. However, in group 2, the strategy used was to ultrafiltrate the prime, add 1000 mL of Ringer's solution and then remove the same amount. A sample was then taken for laboratory analysis.

Table 1 **Demographic and intraoperative data of the study population.**

Variable	Group 1 (23)	Group 2 (32)	P
Age (in years)	2.00 (0.2 – 10)	1.9 (0.6 – 8)	0.183 [1]
Sex (male)	10 (43.5%)	19 (59.4%)	0.244 [2]
Weight (kg)	12 (5 – 25)	9.1(4 – 25)	0.183 [1]
Surgery time (min)	210 (120 – 360)	195 (130 – 405)	0.516 [1]
CPB time (min)	90 (30 – 200)	72 (45 – 165)	0.706 [1]
Anoxia time (min)	55 (17 – 140)	48 (21 – 107)	0.824 [1]
Procedure			
ASD	3 (13%)	4 (12.5%)	0.225 [2]
VSD	15 (65.2%)	26 (81.3%)	
AVSD Total	5 (21.7%)	2 (6.3%)	

CPB: cardiopulmonary bypass; ASD: atrial septal defects; VSD: ventricular septal defects; AVSD Total: atrioventricular septal defect.
1 - Mann-Whitney test, 2 - Chi-square

Table 2 **Postoperative clinical results**

Variable	Group 1 (23)	Group 2 (32)	P*
MV time (hours)	11 (2 – 240)	9.5 (3 – 74)	0.669
ICU time (days)	3 (2 – 28)	3 (2 – 27)	0.816
Total length of stay (days)	13 (6 – 35)	9 (6 – 34)	0.032

MV: mechanical ventilation; ICU: intensive care unit.
*Mann-Whitney test

Table 3 **Laboratory data of the initial prime of groups 1 and 2**

Variable	Group 1 (23) Prime	Group 2 (32) Prime (pre-UF)	P*
Glucose (mg/dL)	84 (44 – 152)	112 (65 – 161)	0.008
Sodium (mmol/L)	152 (146 – 160)	141.5 (135- 150)	<0.001
Potassium (mmol/L)	6.1 (4.6 – 9.4)	7.6 (2.7 –14.3)	0.006
Lactate (mmol/L)	4.1 (2.1 – 6.6)	4.6 (2.5 – 7.3)	0.322

mg/dL:: milligrams per deciliter; mmol/L: millimoles per liter.
*Mann-Whitney test

Table 4 **Laboratory data before and after blood prime ultrafiltration in group 2**

Variable	Group 2 (32) Prime (pre-UF)	Group 2 (32) Prime (post-UF)	P*
Glucose (mg/dL)	112 (65 – 161)	51 (28 – 105)	< 0.001
Sodium (mmol/L)	141.5 (135 – 150)	160.5 (152 -168)	< 0.001
Potassium (mmol/L)	.7,6 (2.7 – 14.3)	3.1 (1.2 – 6.9)	< 0.001
Lactate (mmol/L)	4.6 (2.5 – 7.3)	2.5 (1.4 – 5.6)	< 0.001

pre-UF: pre-ultrafiltration; post-UF: post-ultrafiltration; mg/dL: milligrams per deciliter; mmol/L: millimoles per liter
*Mann-Whitney test

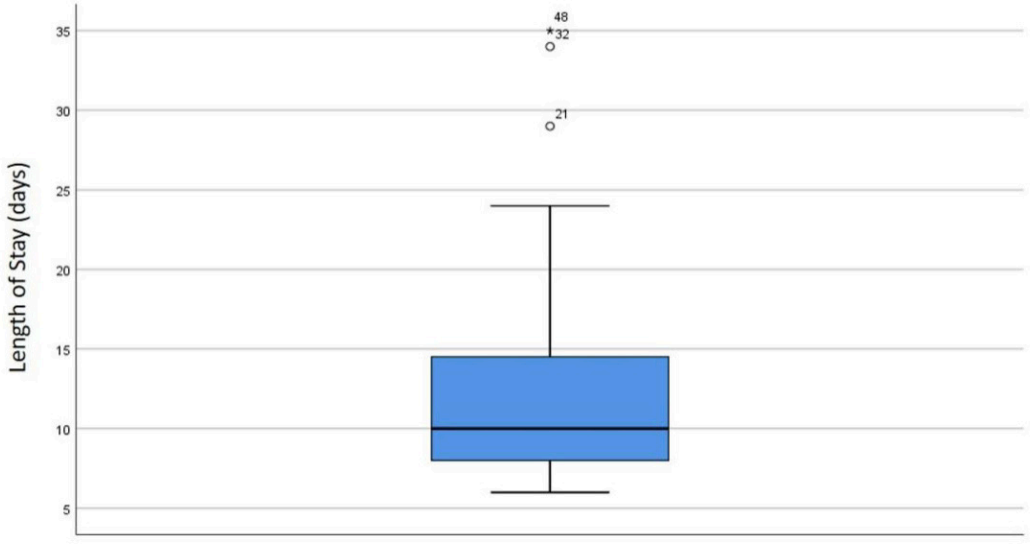

Figure 1 *Boxplot representing the distribution of hospital length of stay. The box limits indicate the first (Q1) and third (Q3) quartiles; the central line represents the median. Points outside the "whiskers" are considered outliers (atypical values).*

Table 5 **Laboratory data of the prime of group 1 and the post-ultrafiltration prime of group 2 (unchanged for group 1) before the start of CPB**

Variable	Group 2 (32) Prime (pre-UF)	Group 2 (32) Prime (post-UF)	P*
Glucose (mg/dL)	84 (44 -152)	51 (28 – 105)	< 0.001
Sodium (mmol/L)	152 (146 – 160)	160.5 (152 -168)	< 0.001
Potassium (mmol/L)	6.1 (4.6 – 9.4)	3.1 (1.2 – 6.9)	< 0.001
Lactate (mmol/L)	4.1 (2.1 – 6.6)	2.5 (1.4 – 5.6)	< 0.001

post-UF: post-ultrafiltration; mg/dL: milligrams per deciliter; mmol/L: millimoles per liter
*Mann-Whitney test

Laboratory blood analysis

The blood samples for laboratory analysis were taken via the patient's arterial catheter and the collections were divided into 4 times:

T1: after induction of anesthesia;

T2: at the beginning of CPB, before clamping the aorta;

T3: at the end of CPB, after rewarming;

T4: at the end of the surgical procedure.

In the immediate postoperative period (IPO), further blood samples were taken at 2 different times:

IPO1: after admission to the intensive care unit (ICU);

IPO2: 24 hours after operation.

Blood samples collected for arterial blood gas analysis were analyzed using a GEM® Premier™ 4000 automated analyzer. This analyzer measured the concentration of glucose (mg/dL), sodium (mmol/L), potassium (mmol/L) and lactate (mmol/L).

Comprehensive patient information was collected, including individual characteristics, preoperative data, type of surgery performed, cardiopulmonary bypass parameters, mortality, duration of mechanical ventilation, ICU stay and length of postoperative hospitalization.

Statistical analysis

All samples included in this study were subjected to detailed statistical analysis using the SPSS version 25.0 program. The assessment of normality of the data, which is crucial for the identification of significant differences ($p<0.05$) between the data sets, was performed using the Shapiro-Wilk test. Data that met the criteria for normal distribution were presented as mean ± standard deviation, while medians (interquartile range) were used for variables that were not normally distributed.

Table 6 **Comparison of laboratory levels of group 1 and group 2 at intraoperative moments.**

Variable		T1	T2	T3	T4
Glucose (mg/dL)	1	85 (49 – 132)	97 (60 – 139)	116 (55 – 198)	151 (75 – 236)
	2	88.5 (65 – 131)	93 (44 – 154)	115.5 (68 – 221)	132 (44 – 230)
P *		0.278	0.834	0.878	0.093
Sodium (mmol/L)	1	134 (131 – 140)	139 (134 – 152)	142 (136 – 149)	144 (136 – 150)
	2	134 (130 – 138)	138 (128 – 145)	143 (136 – 149)	143 (137 – 149)
P *		0.289	0.487	0.342	0.734
Potassium (mmol/L)	1	3.7 (2.8 – 4.4)	4.0 (2.9 – 5.1)	3.8 (2.9 – 5.3)	3.7 (2.9 – 4.7)
	2	3.8 (3.1 – 4.7)	3.4 (2.7 – 4.6)	3.8 (2.5 – 5.1)	3.8 (2.9 – 5.2)
P *		0.35	<0.001	0.688	0.461
Lactate (mmol/L)	1	1.0 (0.6 – 1.8)	1.6 (1.0 – 3.1)	1.6 (0.9 – 3.7)	2.2 (1.0 – 5.0)
	2	0.9 (0.5 – 2.2)	1.5 (0.9 – 4.1)	1.1 (0.6 – 3.8)	1.5 (0.7 – 5.4)
P *		0.648	0.134	0.013	<0.001
Hematocrit (%)	1	32.0 (23 – 41)	29.0 (23 –36)	29.0 (25 –39)	38.0 (31 –47)
	2	32.0 (25 –39)	28.5 (21 –33)	27.0 (24 –34)	38.0 (26 –48)
P *		0,492	0,167	< 0,001	0,386

mg/dL: milligrams per deciliter; mmol/L: millimoles per liter; induction of anesthesia (T1); before aortic clamping (T2); rewarming of the patient on CPB (T3); end of the surgical procedure (T4).
*Mann-Whitney test

Table 7 **Comparison of the laboratory levels of group 1 and group 2 at postoperative periods**

Variable		IPO(1)	IPO(2)
Glucose (mg/dL)	1	130 (83 – 258)	101 (59 – 138)
	2	124.5 (44 – 216)	106 (65 – 230)
P *		0.851	0.532
Sodium (mmol/L)	1	146 (139 – 166)	141 (134 – 159)
	2	145.5 (138 – 153)	140 (134 – 160)
P *		0.986	0.771
Potassium (mmol/L)	1	3.3 (2.7 – 4.6)	3.5 (2.6 – 4.4)
	2	3.4 (2.2 – 4.8)	3.3 (2.6 – 4.4)
P *		0.914	0.065
Lactate (mmol/L)	1	2.2 (1.3 – 4.5)	1.5 (1.0 – 2.3)
	2	1.7 (0.9 – 5.3)	1.5 (0.8 – 4.0)
P *		0.008	0.891

mg/dL: milligrams per deciliter; mmol/L: millimoles per liter; IPO: immediate postoperative period; admission to the ICU (IPO1); 24 hours postoperatively (IPO2).
*Mann-Whitney test

Comparisons between groups were performed with methodological rigor using Student's t-test for interval data with normal distribution. If the normal distribution was not met, the Mann-Whitney test for interval data was used. In addition, Pearson's chi-square test was used to assess associations between qualitative variables.

RESULTS

In the period from March 2022 to October 2023, 55 elective congenital heart surgery patients were enrolled and completed the research protocol. Of these, 23 (41.8%) were from group 1 and 32 (58.2%) from group 2. The proportion of male patients was 43.5% in group 1 and 59.4% in group 2. The proportion of females was 56.5% in group 1 and 40.6% in group 2. There were no significant differences between the groups in terms of age, weight, surgery, CPB and anoxia time. Regarding the surgical procedure, ventricular septal defect repair was the most frequently performed procedure in both groups, with 15 patients (65.2%) in group 1 and 26 patients (81.3%) in group 2 (Table 1).

Clinical outcomes

There was no difference between the groups in terms of MV time and length of stay in the ICU. However, the median value for length of hospital stay was higher in group 1 than in group 2 [13 (6 - 35) vs 9 (6 - 34); p= 0.032]. There were no deaths among the 55 participants during the time they were in the study (Table 2). Hospital stay duration was also assessed graphically using a boxplot (Figure 1). Despite similar interquartile ranges between the groups, a significant difference in medians was observed. The boxplot highlighted the presence of outliers at 21, 32, and 48 days, contributing to greater variability. These findings support the use of the median as a more appropriate measure of central tendency for this variable due to the skewed distribution.

Laboratory outcomes

As shown in Table 3, the values were compared between group 1 (prime) and group 2 (pre-UF): glucose (p= 0.008), sodium (p= < 0.001), potassium (p= 0.006) and lactate (p= 0.322). Initial blood glucose and potassium levels in the CPB circuit were higher in group 2. Conversely, sodium levels were higher in group 1, while lactate levels showed no difference between the groups.

Group 2 showed a significant difference when comparing the blood prime before and after ultrafiltration. The values for glucose, potassium and lactate decreased, while sodium increased in the post-UF sample (p=<0.001) (Table 4).

In Table 5, groups 1 and 2 showed a difference in the prime before starting CPB for the values of glucose, sodium, and potassium (p= <0.001) and lactate (p= 0.001).

Table 6 shows that the patients' glucose, sodium, potassium and lactate levels during induction of anesthesia showed no differences between the groups. It was observed that glucose levels tended to increase intraoperatively, but with no significant differences between groups. Sodium levels remained constant across all time points and showed no fluctuations. At time point T2, a difference in potassium levels was found between group 1 and group 2 [4.0 (2.9–5.1) vs 3.4 (2.7–4.6), p= < 0.001]. Significant differences were observed in lactate levels at time points T3 [1.6 (0.9–3.7) vs 1.1 (0.6–3.8), p= 0.013] and T4 [2.2 (1.0–5.0) vs 1.5 (0.7–5.4), p= < 0.001]. In some samples, the lowest hematocrit levels during CPB were 23.0% in Group 1 [29.0 (23–36)] and 21.0% in Group 2 [28.5 (21–33)], both occurring in the early CPB phase T2.In IPO (1), lactate levels differed between group 1 and group 2 [2.2 (1.3–4.5) vs 1.7 (0.9–5.3), p= 0.008]. In IPO (2), however, these values normalized [1.5 (1.0–2.3) vs 1.5 (0.8–4.0), p= 0.891] (Table 7).

DISCUSSION

Ultrafiltration of CPB blood prime not only offers the possibility of extracting waste products and unwanted metabolites from the stored RBC, but also proves to be a versatile tool for providing more physiological electrolyte values.

The values in the standard blood sample obtained in the CPB circuit showed differences. It is important to note that patients in group 1 had a higher median weight compared to group 2 [12 (5–25) vs 9.1 (4–25), p= 0.183]. The volume of the venous reservoir of the LILLIPUT 1 and KIDS D101 circuits was 425 mL and 1500 mL, respectively. Patients in group 1 therefore used circuits with a larger volume. The different amount of crystalloids used together with the packed red blood cells may have influenced the results, especially with regard to glucose, sodium and potassium levels. It was observed that glucose levels were lower in group 1, while sodium levels were higher. An increase in the volume of crystalloid fluids may have diluted the glucose concentration in the first phase, while the sodium may have contributed to its increase.

Shimpo et al. [17], in their study of pediatric patients, showed a decrease in sodium and potassium levels after ultrafiltration of blood prime in one of the groups studied. Gholampour et al.[18] made it clear that zero-balance ultrafiltration using Ringer's (500 mL) was able to modify and reduce the baseline potassium, sodium, glucose, and lactate values of the prime of the CPB circuit. The results of this study corroborate the findings of Gholampour et al.[18] and Shimpo et al .[17] because in group 2 the pre- and post-UF prime values differed, with a reduction in potassium, glucose, and lactate values. However, when it came to sodium values, an increase was noted. Osthaus et al. [19] used 1000 mL of a crystalloid solution buffered with bicarbonate in their study, causing an increase in sodium values after ultrafiltration. The greater quantity of crystalloid solution used may be responsible for the increase in sodium values, since in this study a quantity of 1000 mL of Ringer's was used as the wash volume. Confirming the findings of the present study, Ugaki et al. [12] in their in vivo study with an animal model, showed higher sodium values

post-ultrafiltration than pre-ultrafiltration, although there was no significant difference in the results, showing that the amount of 1500 mL of Ringer's lactate used to wash the blood prime may have influenced these values.

Clinical outcomes

When examining the clinical outcomes, the results presented show that there were no significant differences between group 1 and group 2 in terms of time spent on mechanical ventilation and length of stay in the ICU, indicating a similarity in these aspects. Kohlsaat et al. [20] also found no difference in their results regarding the length of mechanical ventilation, length of ICU stay, and hospital stay in pediatric patients undergoing cardiac surgery with blood prime. Nagashima et al. [21] revealed in their findings that the initial ultrafiltration technique reduced pulmonary dysfunction and mechanical ventilation time. Gholampour et al. [22] showed that the group in which zero prime blood balance was performed had a faster extubation time compared to the control group and that the length of stay in the ICU was shorter for patients in the latter group.

However, when comparing hospitalization durations in this study, group 1 presented a higher median length of stay than group 2. This difference was statistically significant ($p = 0.032$), suggesting a potential influence of specific factors in group 1 that may prolong hospital stays. The presence of extreme values, as demonstrated in the boxplot, underscores the importance of using robust descriptive measures, such as the median, in the context of asymmetric distributions. These outliers likely reflect individual clinical complications or particular patient profiles, and their identification is essential for accurate interpretation. Despite similar interquartile ranges between groups, the significant difference in medians remains relevant and is reinforced by the graphical analysis.

Gholampour et al. [22] suggest that the blood prime ultrafiltration technique reduces the risk of lesions induced by inflammatory mediators, as well as preventing an increase in these factors during and after CPB. Nagashima et al. [21] reported that the initial reduction of the inflammatory response at the beginning of CPB may influence the attenuation of subsequent reactions, rather than directly removing all inflammatory mediators in the ultrafiltration of the initial prime. The study by Nagashima et al.[21] suggests that the recirculation of blood in the CPB circuit before connection to the patient, together with hemofiltration, can consume the substrates of inflammation. This was proven by the significant decrease in the concentration of kininogen in the prime, which may be due to its consumption and adhesion to the circuit, and not due to hemofiltration and removal. This hypothesis is due to the lack of change in the values of albumin, which has a molecular weight of (70kDa), and kininogen, (78kDa), which should not be removed. Furthermore, other explanations for this are that the long recirculation of the prime may somehow improve the biocompatibility of the circuit surface. Thus, at the beginning of CPB, a layer of protein can suppress the inflammatory activation generated by contact with the patient's blood. What could explain the lack of clinical difference between the groups in this study is the assumption that both group 1 and group 2 had the same length of time the prime was circulating in the circuit.

It is encouraging to note that there were no deaths during the research period, reflecting the safety and efficacy of the procedure for patients. This data reinforces the importance of continuous research and the application of strategies that contribute to the safety of patients undergoing congenital heart surgery. On the other hand, Kohlsaat et al. [20], in their study, found a 4% mortality rate in each group investigated; however, this result is not statistically significant. It is worth noting that the number of participants was 1,121 people, a larger number than in this survey.

Intraoperative laboratory outcomes

The initial results of the patients after induction of anesthesia show that the values were within the reference parameters, with no statistically significant difference between the groups. This initial homogeneity is crucial to ensure that the differences observed later are not due to a different baseline between the groups.

Throughout the surgical procedure, samples collected during induction of anesthesia, cardiopulmonary bypass and at the end of surgery (T1, T2, T3 and T4) showed no significant variation in blood tests. There were no significant fluctuations in the blood analyses, indicating a general stability of the patient's condition during the intraoperative period.

A tendency to increase glucose levels was observed, but this change showed no difference between the groups, suggesting that both responded similarly to this particular aspect. This trend continued in the postoperative period when samples were taken for laboratory analysis on the patient's arrival in the ICU. However, after 24 hours of hospitalization, the values decreased and returned to their original normal value. In contrast, Gholampour et al.[18] showed in their study that glucose levels were significantly lower in the group that underwent primary ultrafiltration. These results were observed in the period after aortic clamping and at the end of CPB.

Hyperglycemia during cardiac surgery is the result of many factors. Surgical trauma is one of these factors, but specific aspects of CPB, such as heparinization, hypothermia, and rewarming at the end of the procedure, also play an important role in elevating blood glucose. During hypothermic CPB, there is a marked increase in concentrations of catecholamines, cortisol and glucagon, triggering a cascade of physiological events. These events include the stimulation of hepatic glycogenolysis, the promotion of gluconeogenesis and an increase in hepatic glucose production. At the same time, total glucose uptake by the body decreases, while renal absorption of filtered glucose is increased. It is important to note that the presence of these hypothermic factors not only promotes circulating glucose, but also has an inhibitory effect on the activity of exogenous insulin. [23]

Blood transfusions can induce acute hyperkalemia, causing adverse cardiovascular effects and electrophysiologic disturbances. Several factors such as transfusion volume and

rate, duration of blood storage and red blood cell irradiation are considered risk factors for these complications, although the exact risk is still unclear.[24]

Sodium values showed consistent stability at all times, with no variations observed until the end of CPB. Even after arrival in the ICU and after 24 hours of IPO, sodium remained stable in both groups. About potassium, a significant difference in values was noted in the T2 period, with a slight increase in potassium in group 1 over group 2 [4.0 (2.9 - 5.1) vs 3.4(2.7 - 4.6), p=<0.001], with no values outside the physiological curve being observed. Potassium maintained a stable trend during the other intraoperative periods, T3 [3.8 (2.9 - 5.3) vs 3.8 (2.5 - 5.1), p= 0.688], T4 [3.7 (2.9 - 4.7) vs 3.8 (2.9 - 5.2), p= 0.461], and in the period corresponding to IPO1 [3.3 (2.7 - 4.6) vs 3.4 (2.2 - 4.8), p= 0.914] and IPO2 [3.5 (2.6 - 4.4) vs 3.3 (2.6 - 4.4), p= 0.065]. These findings are similar to those of Kohlsaat et al. [22], where potassium levels in the first sample collected during CPB showed lower values in the ultrafiltration group than in the control group and, at the end of CPB, these differences became balanced with similar potassium values in both groups.

Differences in lactate levels were observed at the time of patient rewarming (T3) and the end of surgery (T4), and at both times group 1 had higher values compared to group 2 [1.6 (0.9 - 3.7) vs 1.10 (0.6 - 3.8), p= 0.013], [2.2 (1.0 - 5.0) vs 1.5 (0.7 - 5.4), p= <0.001]. After arrival in the ICU, the values continued to show a difference between the groups, but within 24 hours of IPO, stabilization was observed between the groups [1.5 (1.0 - 2.3) vs 1.5 (0.8 - 4.0), p= 0.891], indicating that, despite the initial differences, both groups converged on similar values after this period. It was noted in this study that the group that underwent prime ultrafiltration had lower lactate values, while the group that did not undergo the procedure maintained higher laboratory lactate values until they arrived in the ICU. This shows that prime ultrafiltration can reduce the high levels of lactate present in the red blood cell concentrate, as well as have a positive influence on reducing hyperlactatemia in the results during surgery. The stability of values in the post-operative period suggests an adaptive response or metabolic normalization over time.

Median hematocrit values remained within the recommended target range during cardiopulmonary bypass in both groups. However, some samples showed minimum values of 23% in group 1 [29.0 (23–36)] and 21% in group 2 [28.5 (21–33)]. These episodes of hemodilution occurred predominantly during the early phases of circulation but were not associated with immediate clinical repercussions. Considering that, overall, all intraoperative measurements remained above 25%, these isolated variations are regarded as physiologically tolerable, provided they are accompanied by hemodynamic stability and adequate tissue oxygenation. Nevertheless, strict monitoring of HCT during the initial phases of CPB is essential to avoid critical hemodilution. Soliman et al. [25] highlight that levels below 25% increase the risk of neurocognitive dysfunction, while Ramakrishnan et al. [26] associate values close to 33% with improved clinical outcomes in neonates and infants.

In short, the data shown indicates general stability in the parameters analyzed, with some differences in potassium and lactate levels at some specific times.

Limitations

It is important to note that this study did not reach the initial sample number calculated. This limitation was due to factors such as the high complexity of the cases, where many children did not meet the inclusion criteria. The logistics of the center where the research took place made it difficult to collect data from many patients, and the choice of only ASD, VSD, and AVSD Total correction procedures also influenced the study's limitations. As the hospital is a public institute specializing in cardiovascular diseases, the demand for patients is greater and, concomitantly, there is a multiplicity of cases. Ideally, all patients undergoing surgery would have been included in the study, which would have helped to arrive at the calculated sample size. Nevertheless, despite the restriction of the study population, this research succeeded in achieving the general objective proposed. The results obtained are in line with previous studies, with results that correlate with ones in which the number of patients was higher than those studied here.

It is worth noting that future research could focus on performing more detailed analyses of inflammatory mediators in the prime fluid before and after ultrafiltration, as well as assessing the initial inflammatory response during the CPB period. In addition, it would be valuable to investigate the effects of blood recirculation on the biocompatibility of the artificial surface, including analysis of changes in the composition and structure of the hemoconcentrator membranes and the CPB circuit. These investigations could provide insights into the underlying mechanisms that determine the efficacy of prime-ultrafiltration and help optimise its clinical application to improve outcomes.

During surgery, median hematocrit values remained within the target range in both groups, with a postoperative increase possibly related to ultrafiltration, autotransfusion, or transfusions. However, due to lack of systematic records, the exact cause cannot be confirmed. Additionally, missing data on transfusions and vasoactive or inotropic support limits interpretation. Future studies should adopt more detailed protocols to address these variables.

CONCLUSION

The analysis of intra and postoperative laboratory results showed a general stability of blood parameters, with some fluctuations in potassium and lactate levels. When examining the clinical outcomes, the lack of significant differences in the duration of mechanical ventilation and ICU stay emphasizes the similarities in these postoperative dimensions. However, the observed reduction in hospital length of stay in the group receiving prime ultrafiltration suggests that this technique may help shorten the hospitalization period. In conclusion, the results of this study improve the understanding of initial blood ultrafiltration in the CPB circuit and provide valuable insights for future practice.

REFERENCES

1. Aragão JA, Mendonça MP, Silva MS, et al. The epidemiological profile of patients with congenital heart disease undergoing surgery in the heart hospital. Rev Bras Ciênc Saúde. 2013;17(3):263-8. https://doi.org/10.4034/RBCS.2013.17.03.08
2. Rosa RCM, Rosa RFM, Zen PRG, et al. Cardiopatias congênitas e malformações extracardíacas. Rev Paul Pediatr. 2013;31:243-251. https://doi.org/10.1590/S0103-05822013000200017
3. Belo WA, Oselame GB, Neves EB. Perfil clínico-hospitalar de crianças com cardiopatia congênita. Cad Saude Colet. 2016;24(2):216-20. http://doi.org/10.1590/1414-462X201600020258
4. Souza PC, Gigoski VS, Etges CL, et al. Findings of postoperative clinical assessment of swallowing in infants with congenital heart defect. Codas. 2018;30(1):1-8. http://doi.org/10.1590/2317-1782/20182017024
5. Born D. Cardiopatia congênita. Arq Bras Cardiol. 2009;93(6):130-132. https://doi.org/10.1590/S0066-782X2009001300008
6. Malta DC, Duarte EC, Escalante JJC, et al. Mortes evitáveis em menores de um ano, Brasil, 1997 a 2006: contribuições para a avaliação de desempenho do Sistema Único de Saúde. Cad Saúde Pública. 2010;26(3):481– 491. https://doi.org/10.1590/S0102-311X2010000300006
7. Borghi-Silva A, Mendes RG, Costa FS, et al. The influences of positive end expiratory pressure (PEEP) associated with physiotherapy intervention in phase I cardiac rehabilitation. Clinics. 2005;60(6):465-472. https://doi.org/10.1590/S1807-59322005000600007
8. Schaan CW, Feltez G, Schaan BD, et al. Functional capacity in children and adolescents with congenital heart disease. Rev paul pediatr. 2019;37(1):65-72 https://doi.org/10.1590/1984-0462/;2019;37;1;00016
9. Golab HD, Bogers JJ. Small, smaller, smallest. Steps towards bloodless neonatal and infant cardiopulmonary bypass. Perfusion. 2009;24(4):239-242. https://doi.org/10.1177/0267659109348722
10. Golab HD, Takkenberg JJ, Bogers AJ. Specific requirements for bloodless cardiopulmonary bypass in neonates and infants; a review. Perfusion. 2010 Jul;25(4):237-43. https://doi.org/10.1177/0267659110375862
11. Pouard P. Le priming en CEC néonatale et pédiatrique. IRBM. 2010;31:27-30. https://doi.org/10.1016/S1959-0318(10)70006-3
12. Ugaki S, Honjo O, Kotani Y, et al. Ultrafiltration of priming blood before cardiopulmonary bypass attenuates inflammatory response and maintains cardiopulmonary function in neonatal piglets. ASAIO J. 2009;55(3):291-5. https://doi.org/10.1097/MAT.0b013e31819b00c2
13. Sasaki J, Tirotta C, Lim H, et al. Comparison of stored red blood cell washing techniques for priming extracorporeal circuits. Perfusion. 2018;33(2):130-135. https://doi.org/10.1177/0267659117730134
14. Cedric M, Brian WM, Ines BM, et al. Longer blood storage is associated with suboptimal outcomes in high-risk pediatric cardiac surgery. Ann Thorac Surg. 2012;93(5):1563–1569. https://doi.org/10.1016/j.athoracsur.2011.08.075
15. Sturmer D, Beaty C, Clingan S, et al. Recent innovations in perfusion and cardiopulmonary bypass for neonatal and infant cardiac surgery. Transl pediatr. 2018;7(2):139–150. https://doi.org/10.21037/tp.2018.03.05
16. Delaney M, Axdorff-Dickey RL, Crockett GI, et al. Risk of extracorporeal life support circuit-related hyperkalemia is reduced by prebypass ultrafiltration. Pediatr Crit Care Med. 2013;14(6):263-267. https://doi.org/10.1097/PCC.0b013e31828a70c5
17. Shimpo H, Shimamoto A, Sawamura Y. et al. Ultrafiltration of the priming blood before cardiopulmonary bypass attenuates inflammatory response and improves postoperative clinical course in pediatric patients. Shock. 2001;16(1):51-4. https://doi.org/10.1097/00024382-200116001-00010
18. Gholampour DM, Niknam S, Bakhshandeh H. et al. Zero-balance ultrafiltration of the priming blood modifies the priming components and improves the clinical outcome in infants undergoing cardiopulmonary bypass: A randomized controlled trial. Artif Organs. 2020;44(3):288-295. https://doi.org/10.1111/aor.13559
19. Osthaus WA, Sievers J, Breymann T, Suempelmann R. Bicarbonate buffered ultrafiltration leads to a physiologic priming solution in pediatric cardiac surgery. Interact Cardiovasc Thorac Surg. 2008;7(6):969–972. https://doi.org/10.1510/icvts.2008.179333
20. Kohlsaat K, Gauvreau K, Fynn-Thompson F. et al. Impact of pre-bypass ultrafiltration on prime values and clinical outcomes in neonatal and infant cardiopulmonary bypass. J Extra Corpor Technol. 2023;55(4):175-184. https://doi.org/10.1051/ject/2023039
21. Nagashima M, Imai Y, Seo K. et al. Effect of hemofiltrated whole blood pump priming on hemodynamics and respiratory function after the arterial switch operation in neonates. Ann Thorac Surg. 2000;70(6):1901-6. https://doi.org/10.1016/s0003-4975(00)02024-5
22. Gholampour DM, Niknam S, Azarfarin R. et al. Zero-Balance Ultrafiltration of Priming Blood Attenuates Procalcitonin and Improves the Respiratory Function in Infants After Cardiopulmonary Bypass: A Randomized Controlled Trial Artif Organs. 2019;43(2):167-172. https://doi.org/10.1111/aor.13325
23. Sonkusale M, Zanwar YN, Kane D, Patwardhan AM. Blood glucose monitoring in pediatric patients on cardiopulmonary bypass. Int J Contemp Pediatr. 2016;3:530-6 https://doi.org/10.18203/2349-3291.ijcp20161032
24. Burke M. et al. Transfusion-associated hyperkalemic cardiac arrest in neonatal, infant, and pediatric patients. Front Pediatr. 2021;9:765306. https://doi.org/10.3389/fped.2021.765306
25. Soliman R, Saad D, Abukhudair W, et al. The neurocognitive outcomes of hemodilution in adult patients undergoing coronary artery bypass grafting using cardiopulmonary bypass. Ann Card Anaesth. 2022;25(2):133-140. https://doi.org/doi:10.4103/aca.aca_206_20
26. Ramakrishnan K, Kumar TS, Boston US, et al. Cardiopulmonary bypass in neonates and infants: advantages of high flow high hematocrit bypass strategy—clinical practice review. Transl Pediatr 2023;12(7):1431-1438. https://doi:10.21037/tp-23-94